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(54) Title: METHOD FOR PREVENTING DIET-INDUCED CARNITINE DEFICIENCY IN DOMESTICATED DOGS AND CATS

(57) Abstract

A method is described for increasing the plasma L-Carnitine level in pets. A daily prophylactic amount of L-Carnitine is administered to the pet either as a dietary supplement in an amount of 0.2to 2.0 grams of L-Carnitine per day, or L-Carnitine is provided as an additional ingredient to a commercial pet food in an amount of 0.2 to 2.0 grams of L-Carnitine per kilogram pet food.

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METHOD FOR PREVENTING DIET-INDUCED CARNITINE DEFICIENCY IN DOMESTICATED DOGS AND CATS

General Field of the Invention:

The invention relates to the field of pet food compositions and more specifically to pet food enriched with L-Carnitine.

Background of the Invention:

L-Carnitine is a quaternary amine that promotes beta-oxidation of long-chain fatty acids by facilitating their transfer across the mitochondrial membrane. L-Carnitine has also been shown to promote oxidation of branched-chain amino acids and the utilization of acetyl-coenzyme A.

In mammalian species, L-Carnitine concentration in cardiac and skeletal muscle is much higher than in serum. In these tissues fatty acids are utilized as a major source of energy. Because of L-Carnitine's central role in transporting fatty acids to the site of oxidation, adequate levels of L-Carnitine are required for normal fatty acid and energy metabolism in mammalian hearts. This is evidenced by the restoration to normal of fatty acid oxidation in muscle homogenates of certain L-Carnitine deficient patients. A relationship between deficient levels of myocardial L-Carnitine and cardiomyopathy has been observed in both hamsters and dogs. Restoration toward normal of such deficient L-Carnitine levels has been shown to result in improved myocardial function in both species.

In mammals, L-Carnitine is derived from the diet and from biosynthesis in the liver, and in some species, kidney and other tissues. Neither cardiac nor skeletal muscle is capable of synthesizing L-Carnitine, however. Thus, the L-Carnitine found in these tissues was either absorbed from the diet or biosynthesized endogenously by other tissues.

The present invention is for a method of preventing diet-induced carnitine deficiency in domesticated dogs and cats using a dietary supplement containing a prophylactic amount of L-Carnitine. The invention is useful in preventing L-Carnitine deficiencies which can lead to a multitude of conditions, including myopathic heart disease, ischemic heart disease, hyperlipidemia, ketosis, muscle weakness and premature aging.

Pets, particularly the carnivores, are at great risk for developing L-Carnitine deficiencies. As Table 1 indicates, dog and cat foods are extremely low in free L-Carnitine levels as compared with that found in raw ground beef. Most pets are maintained strictly on commercial pet food diets and are thus kept chronically deficient in L-Carnitine. This results in a diet-induced carnitine deficiency.

TABLE 1

LEVEL OF FREE L-CARNITINE IN PET FOODS

SAMPLE IDENTIFICATION	FREE L-CARNITINE "WATER SOLUBLE FRACTION" nanomoles/gram of product
GROUND BEEF	3000.0
** SAMPLE TYPE : DRY DOG FOOD	
ALPO BEEF FLAVORED DINNER 5LBS	214.2
CARNATION COME N GET IT 4LBS	53.6
GAINES GRAVY TRAIN BEEF FLAVOR 5LBS	89.4
KALKAN MEALTIME SMALL CRUNCHY BITS 5LBS	105.9
KEN-L-RATION LOVE ME TENDER CHUNKS-BEEF	27.3
KEN-L-RATION KIBBLES 'N BITS 4LBS	78.6
PETTS BRAND ALL NATURAL (HUBBARD) 4LBS	167.7
PURINA DOG CHOW 5LBS	161.0
PURINA CHUCKWAGON DOG CHOW	72.7
PURINA HI-PRO 5LBS	93.2
PURINA BUTCHER'S BLEND BEEF,BACON,LIVER	106.3
PURINA FIT AND TRIM 4.5LBS	103.9
PURINA PUPPY CHOW 5LBS	136.0
NUTRO MAX PUPPY KIBBLE PUPPY FOOD	143.5
NUTRO MAX KIBBLE DOG FOOD	192.7
IAMS MINI CHUNKS	182.9
EUKANUBA (BY IAMS)	216.3
** SAMPLE TYPE : SEMI-MOIST DOG FOOD	
GAINES BURGERS - BEEF 36OZ	55.5
KEN-L-RATION SPECIAL CUTS 24OZ	59.2
** SAMPLE TYPE : CANNED DOG FOOD	
ALPO BEEF & LIVER DINNER 14OZ	222.8
ALPO LAMB CHUNKS	89.2
CARNATION MIGHTY DOG BEEF 6.5OZ	1799.1
CARNATION MIGHTY DOG TURKEY&GIBLETS	172.3
GAINES CYCLE 2 (ADULT) BEEF 14OZ	28.6
GAINES CYCLE 1 (PUPPY) 14OZ	208.9
KALKAN CHOPPED MEATY COMBO 14OZ	129.7
KEN-L-RATION CHICKEN,BEEF,LIVER DINNER	33.9
KEN-L-RATION CHICKEN DINNER	30.2
RECIPE HEARTY MEAT DINNER 14OZ	95.5
VETS-BEEF FLAVORED 15OZ	62.5
** SAMPLE TYPE : DRY CAT FOOD	
KALKAN CRAVE 18OZ	135.7
CARNATION FRISKIES OCEAN FISH FLAVOR	168.6
STARKIST 9 LIVES CRUNCHY MEALS REAL TUNA & EGG	114.0

IAMS CAT FOOD 26OZ	196.9
PURINA CAT CHOW 22OZ	109.1
PURINA KITTEN CHOW 18OZ	121.4
PURINA MEOW MIX 18OZ	61.2
PURINA TENDER VITTLES MOIST CHICKEN DINNER	127.8
PURINA THRIVE 18OZ	95.2
PURINA SPECIAL DINNERS SEA NIP DINNER 18OZ	188.2
** SAMPLE TYPE : CANNED CAT FOOD	
STARKIST AMORE TURKEY&GIBLET DINNER 3OZ	94.0
STARKIST AMORE POACHED SALMON DINNER 3OZ	101.2
CARNATION FRISKIES BUFFET TURKEY&GIBLET 6OZ	80.0
CARNATION FRISKIES BUFFET SEAFOOD SUPPER 6OZ	180.5
CARNATION FANCY FEAST BEEF&LIVER GOURMET 3OZ	364.6
CARNATION FANCY FEAST FANCY SEAFOOD FEAST 3OZ	115.4
KALKAN TENDER TURKEY DINNER 6OZ	142.0
STARKIST 9 LIVES LIVER&CHICKEN DINNER 6OZ	64.5
STARKIST 9 LIVES OCEAN WHITEFISH DINNER 6OZ	134.3
PURINA 100 TUNA 6OZ	294.3
PURINA BEEF & LIVER DINNER 6OZ	595.6

Example 1

Six apparently healthy Greyhound dogs were determined to be normal by physical examination, fecal flotation, complete blood count, serum biochemical profile, ECG, and echocardiography. They were fed a standard commercial dog food diet free choice for a one-month control period. Control plasma samples (as well as subsequent test samples) were obtained following an eight-hour fast on two consecutive days for analysis of total, free, and esterified L-Carnitine concentration. The average of the plasma L-Carnitine concentration on two consecutive days was taken for each dog and each measuring period.

Following the control period, all of the dogs were continued for two weeks on the standard commercial dog food

diet supplemented with L-Carnitine. The L-Carnitine supplement was in the form of 0.5kg per dog per day of raw frozen lean ground beef. This was equivalent to a daily supplement of 350 mg. of L-Carnitine per dog. Plasma samples were drawn on days 7 and 8 (averaged for the one-week measurement) and days 13 and 14 (averaged for the two-week measurement) for L-Carnitine analysis. Differences between the means of each test period and control were determined by the Student's t test.

Results

The results of the study are shown in Table 2.

TABLE 2

PLASMA CARNITINE CONCENTRATIONS, U MOLES / LITER.

Dog	Control			Week 1			Week 2		
#	Total	Free	Ester	Total	Free	Ester	Total	Free	Ester
1	29.6	25.0	4.5	70.1	58.9	11.2	52.4	44.9	8.0
2	38.7	32.2	6.5	70.7	60.5	10.2	65.7	62.2	3.5
3	27.2	26.1	1.2	57.2	52.5	4.7	58.1	52.7	2.2
4	31.9	30.5	1.4	63.1	55.6	3.4	56.3	52.0	4.3
5	23.1	20.0	3.1	58.1	56.0	2.1	66.3	58.5	8.7
6	27.6	23.4	4.2	56.3	51.7	4.8	43.2	41.0	2.2
AVG	31.8	26.2	3.4	62.5*	55.9**	6.0	57.0	51.9*	4.8
S.D.	±5.0	±4.5	±2.0	±6.5	±3.5	±3.7	±8.6	±8.0	±2.8

Control is after 1 month of commercial dog food only. Week 1 and 2 are after 1 and 2 weeks of ground beef supplementation (0.5kg/day/dog) respectively.
* Denotes statistical significance at $p \leq 0.05$
**Denotes statistical significance at $p \leq 0.01$

The data in Table 2 indicates that the plasma L-Carnitine concentration of a normal, otherwise healthy dog, previously maintained on a commercial pet food diet, is substantially deficient in carnitine as compared with the

plasma carnitine levels found in other mammals. For example, in humans the mean value of plasma total carnitine is 59.3 ± 11.9 μM for males and 51.5 ± 11.6 μM for females. C.J. Rebouche and D.J. Paulson, Carnitine Metabolism and Function in Humans, 6 Ann. Rev. Nutr. pp. 41-66, at page 45. In rats, plasma carnitine concentration averages 56.5 ± 2.2 μM. P.R. Borum, "Regulation of the Carnitine Concentration in Plasma" in Carnitine Biosynthesis, Metabolism, and Functions, 1980, Academic Press, New York, at page 119.

Further, the data of Table 2 indicates that the plasma total L-Carnitine concentration is significantly increased if the animal's diet is supplemented with L-Carnitine and that such level stabilizes in a range that is considered normal when compared with the plasma carnitine levels of other mammals. See Rebouche, supra, and Borum, supra.

It is clearly evident from the foregoing data that supplementation with a prophylactic amount of L-Carnitine of the standard commercial dog food will dramatically increase the plasma concentration of L-Carnitine in dogs. A prophylactic amount is the amount of L-Carnitine required to prevent the animal from developing a diet-induced carnitine deficiency. For a carnivore, such as a dog or cat, this is roughly equivalent to the amount of L-Carnitine the animal would ingest if its diet consisted of red meat, i.e., approximately 700 mg. of L-Carnitine per kilogram of food consumed.

It is to be understood that although the foregoing Example details the use of raw frozen lean ground beef as an L-Carnitine source, other sources within the scope of the claims can be readily utilized in the application of the invention with essentially equivalent results. For example, meat or meat by-products may be used other than raw frozen lean ground beef. These meat or meat by-products may be heat processed, dried or frozen and are suitable substitutes provided such meat or meat by-products have an L-Carnitine concentration in the range of 0.2 to 2.0 grams L-Carnitine per kilogram. The term "meat" is understood to apply not only to the flesh of cattle, but also that of other mammals, poultry and fish. The term "meat by-products" is intended to refer to those non-rendered parts of the carcass of slaughtered animals including but not restricted to mammals, poultry and the like.

Also within the scope of the claims would be the use of commercially prepared L-Carnitine such as that obtained from Austin Chemical Company, Inc., 9655 West Bryn Mawr Avenue, Rosemont, Illinois.

These L-Carnitine supplements may be administered separately in the form of dietary supplements or they may be added at the time of manufacture of the commercial dog food as an additional ingredient in the commercial dog food. If used as a separate dietary supplement, the L-Carnitine may be combined with other valuable nutritional

or prophylactic substances. Examples of this would be a combination of L-Carnitine with a vitamin and mineral preparation. Another example would be the inclusion of a prophylactic amount of L-Carnitine with an anti-heartworm medication such as diethyl-carbamazine.

The L-Carnitine supplement may also be administered as a liquid preparation. L-Carnitine is extremely soluble in water. Such a liquid preparation may be prepared by dissolving the appropriate amount of L-Carnitine in a waterbased solution. Flavoring agents or other nutritional or prophylactic substances may likewise be combined in the solution. The liquid preparation may be administered to the pet separately as a dietary supplement. It may be added to the pet's drinking water or to the animal's food. Further, the concentration of L-Carnitine in the liquid preparation may be such that it may be easily measured out and the prophylactic amount administered to the animal daily.

CLAIMS

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

5. A method for preventing diet-induced carnitine deficiency in a domesticated dog or cat, comprising the step of: administering daily to said dog or cat a prophylactic amount of L-Carnitine.

6. A method as described in claim 5, wherein said L-Carnitine is administered by adding said L-Carnitine to said dog or cat's pet food so as to form a mixture and feeding said mixture to said dog or cat.

7. A method as claimed in claim 6, wherein said mixture has an L-Carnitine concentration of at least 700 mg. L-Carnitine per kilogram mixture.

8. A method as described in claim 5, wherein said L-Carnitine is administered by dissolving said prophylactic amount of L-Carnitine in said dog or cat's drinking water so as to form a solution and feeding said solution to said dog or cat.

9. A method as claimed in claim 8, wherein said solution has an L-Carnitine concentration of at least 700 mg. L-Carnitine per liter of solution.

10. A method as claimed in claim 5, wherein said prophylactic amount is an amount sufficient to produce and maintain in said dog or cat plasma total carnitine concentration of at least 40.0 μM/liter of plasma.

11. A method for preventing diet-induced carnitine deficiency in a domesticated dog or cat comprising the steps of: mixing a sufficient amount of L-Carnitine with said dog or cat's food so as to form a mixture having an L-Carnitine concentration of at least 700 mg. per kilogram of mixture; feeding daily said mixture to said dog or cat.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US89/01808

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC(4): A23K 1/00
U.S.CL.: 426/2

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
U.S.	426/2, 635,646, 805 514/556

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category *	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
X	JP, A, 55-121441 (SHIMAKYU) 27 February 1980 See the Abstract	5-11
A	US, A, 4,656,191 (FANELLI) 07 April 1987	5-11
A	US, A, 4,434,160 (JERETIN) 28 February 1984	5-11
A	US, A, 4,254,147 (CAVAZZA) 03 March 1981	5-11
A	US, A, 4,689,226 (NURMI) 25 August 1987	5-11
A	US, A, 4,702,914 (RYAN) 27 October 1987	5-11

* Special categories of cited documents: [10]

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
22 JUNE 1989	17 JUL 1989
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